Our Thanks to the Schering Corporation

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We salute the Schering Corporation for their contribution to the Endowment Fund and for their continued support of clinical and investigative dermatology.

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In This Issue . . .

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Recognizing Type VII Collagen

Type VII collagen, a protein of epithelial basement membranes, is composed of a trimer of identical α chains. Each polypeptide has a 145-kDa noncollagenous amino-terminal domain and a 145-kDa collagenous carboxy-terminal section. In the December 1992 issue of this journal, Gammon *et al* (J Invest Dermatol 99:691–696, 1992) reported the isolation and characterization of a cDNA encoding the N-terminal noncollagenous (NC1) portion of type VII collagen. Autoantibodies in serum from a patient with epidermolysis bullosa supplied a handle for the cDNA library screening step. This clone provided further information about the structural regions of type VII collagen. The NCl domain contains multiple tandem repeats of fibronectin-like sequences as well as a region that binds type IV collagen and a segment that has homology with von Willebrand factor A. Both epidermolysis bullosa acquisita (EBA) and systemic lupus erythematosus (SLE) are autoimmune blistering disorders. Each is characterized by tissue-bound and circulating IgG autoantibodies that react with collagen in the epithelial basement membrane. In this issue Gammon and his colleagues *(p. 618)* create an epitope map of the NCl domain of type VII collagen and determine the sites where EBA and SLE autoantibodies interact with the protein.

A panel of overlapping cDNA fragments that span the protein coding region was subcloned into two different expression vectors. Each new clone produced a fusion protein containing one or more identified structural elements in NCl. By Western immunoblot and enzyme-linked immunosorbent assays, seven EBA and five SLE patient sera targeted each fusion protein for autoantibody recognition. Because type VII collagen plays a role in lamina densa–dermal adhesion, and because alteration of the Co17A-1 gene in dystrophic forms of EB disrupts formation of anchoring fibrils, the authors reasoned that autoantibodies of EBA and SLE might interfere with adherence by interacting with different epitopes of type VII collagen. The authors make several interesting points. First, all but one (>90%) of the sera containing type VII collagen antibodies react with fusion proteins generated from the NCl domain. Second, most sera recognized at least two regions in the fibronectin-like repeat section. These areas do not share common amino acid sequences and are not cross-reactive, indicating that they are distinct epitopes. Third, no antisera reacted unambiguously with the putative collagen binding domain.

The finding of similar epitope recognition by EBA and SLE autoantibodies suggests that differences in the clinical phenotypes of these disorders do not result from differences in the sites of the collagen VII molecule recognized by the antibodies, and supports previous work by the group indicating that functional heterogeneity among collagen VII autoantibodies may influence clinical phenotype (J Invest Dermatol 89:478–483, 1987). The possibility remains that there are fine differences in precise peptide sequences recognized by these antibodies and the group is currently addressing this question by determining which amino acid sequences are recognized by the autoantibodies.

Another Warning About Alcohol Consumption

Severe psoriasis has been effectively treated with the aromatic retinoid acetretin and its ester, etretinate. The ester is more active and more easily absorbed than acetretin; however, it accumulates in adipose tissues after chronic administration. Because both compounds are potentially teratogenic, acetretin has been favored for treatment of women during their childbearing years because it is more rapidly eliminated from the body. Recently, the 2-month anticonceptive period following acetretin therapy was extended to 2 years after some patients showed elevated plasma levels of etretinate. Preliminary studies in rats showed that ethanol might act as a contributing factor in the esterification of acetretin *in vivo*. To clarify the relationship between plasma levels of these retinoid metabolites and alcohol use, Larsen *et al (p. 623)* monitored 10 patients receiving a 3-month chronic acetretin treatment for psoriasis. Blood

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